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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/413,110	10/06/1999	EVAN C. UNGER	UNGR-1580	1596

7590 11/14/2002

DAVID A CHERRY ESQ  
WOODCOCK WASHBURN KURTZ  
MACKIEWICZ & NORRIS LLP  
ONE LIBERTY PLACE 46TH FLOOR  
PHILADELPHIA, PA 19103

EXAMINER

SHARAREH, SHAHNAM J

ART UNIT PAPER NUMBER

1617

DATE MAILED: 11/14/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/413,110

Applicant(s)

UNGER, EVAN C.

Examiner

Shahnam Sharareh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 116-185 is/are pending in the application.
- 4a) Of the above claim(s) 132-137, 142-145, 152-159, 161-163, 167 and 175-177 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 116-131, 138-141, 146-151, 160, 164, 168-174 and 178-185 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 27, 28
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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PTO-326 (Rev. 04-01)

Office Action Summary

Part of Paper No. 29

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***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 21, 2002 has been entered.

***Status of the Claims***

Claims 116-185 are pending. Claims 132-137, 142-145, 152-159, 161-163, 167, 175-177 are withdrawn as they are directed to nonelected species.

Any rejection that is not addressed in this Office Action is considered obviated in view of the Amendment.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-185 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over patented claims 1-96 of U.S. Patent No. 6,443,898 B1, and claims 1-15 of US Patent 6,416,740 B1, and claims 1-63 of US Patent 6,403,056.

The conflicting claims are not patentably because the patented claims and the pending claims are directed to methods of delivering a bioactive agent in combination with a gaseous liposomal composition and then applying an ultrasounic energy source. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to practice either set of the claims when in possession of the other, because the method steps utilizes similar therapeutic composition and are manipulatively the same.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-185 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 09/075,477, 09/218,660, 09/813,484, 10/055,772.

For the reasons set forth above, the copending claims are also obvious variants of the pending claims in this application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 116-185 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "enhancing" in claim 116, 164 appear to be a relative term which renders the claim indefinite. The term "enhancing" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. To what is the instant method of delivery compared in claiming the enhancing the delivery?

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily

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published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 116-131, 138-140, 160, 164-166, 168-174, and 178-184 stand rejected under 35 U.S.C. 102(b) as being anticipated by Siegel US Patent 5,695,460.

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive. Applicant argues that Siegel methods work because of the increased caviatation of vascular fluid surrounding the thrombosis and Siegel does not define methods for delivering a bioactive agent to a selected tissue. (Amendment, p. 4-5).

In response, Examiner states that the instant claims are directed to methods of enhancing delivery of a bioactive agent comprising (i) administering an agent to a patient, (ii) administering a vesicle composition comprising an aqueous carrier, a gas or gaseous precursor, and vesicles comprising lipids, proteins or polymers to the patient (iii) and applying ultrasonic energy to a tissue to cause cavitations or rupture of said vesicles, wherein the gas comprise a perfluorocarbon. ~~Viewing the claims having their~~ broadest reasonable interpretation in mind, the instant claims are directed to methods of drug delivery to any tissue including tissues with reduced perfusion tissues.

Siegel clearly teaches the compositions and the process steps of the instant claims. (see claims 1-5, Example VII). The cited portions of Siegel, col 5, lines 17-18 and lines 26-28 in the Amendment is only Siegel's description of prior art, and by no means is viewed to be the sole scope of Siegel's invention.

Furthermore, Applicant's assertion that Siegel's invention is not directed to "delivering a bioactive agent" is not persuasive, because under the principles of inherency, a prior art that does not expressly disclose claim limitations anticipates the claims, if it necessarily functions in accordance with, or includes, those limitations. *Atlas Powder Co. v. IRECO Inc.* 190 F.3d 1342, 1349 (Fed. Cir. 1999). Inherency is not necessarily coterminous with knowledge of those of ordinary skill in art, since artisans of ordinary skill may not recognize inherent characteristics or functioning of prior art, but discovery of previously unappreciated property of prior art composition or of scientific explanation for prior art's functioning, does not render old compositions patentably new to discoverer. *Id.* Accordingly, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 630 (Fed. Cir. 1987).

In the instant case, the instant claims use similar method compositions as taught by Siegel. Further, the process steps are essentially the same as those described in Siegel. Siegel in numerous places, discloses the use of a liposomal gaseous contrast agent with a thrombolytic agent such as streptokinase (see Example VII, col 10, lines 20-col 14, lines 50). In fact, not only the contrast agent of Siegel is the same as the instantly employed compositions, but also Siegel employs about the same frequencies as the instant claim 185 (see col 5, lines 29-38).

Further, the recitation that an element is "sufficient" or "capable" to perform a given function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. *In re Hutchinson*, 69 USPQ



138. Accordingly, as the process steps of Siegel are the same as the instantly claimed methods, and the instantly claimed tissue encompasses vascular ischemic tissues; Siegel's delivery of thrombolytics to vascular ischemic tissues anticipates the limitations of the instant claims.

Finally, in response to applicant's argument that Siegel's method is directed to a different purpose, Examiner replies that the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, the process steps of Siegel are the same as the instantly claimed methods. Thus, Siegel anticipates the limitations of the instant claims.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-184 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger et al US Patent 6,443,898.

Unger et al disclose methods of delivering therapeutic compounds to a region of a patient comprising administering to a patient a gaseous filled microspheres comprising a therapeutic compound and the rupturing the microspheres using ultrasound energy (see col 65, lines 15-66; col 66, lines 1-64). Thus, Unger et al anticipate the limitations of the instant claims.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-185 are rejected under 35 U.S.C. 102(e) as being anticipated by Klaveness et al Patent 6,331,289.

Klaveness discloses methods of delivering therapeutically active compositions comprising administering a gaseous contrast agent and a bioactive agent to a subject and then employing ultrasound energy with about 1MHz of frequency, to deliver the

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bioactive agent (see abstract; col 18, lines 59-col 22; col 39-60; see Example 1, col 63-66, for in vivo utility; Examples 17-23, 30,331,5,17-18). Accordingly, Klaveness anticipates the limitations of the instant claims.

Claims 116-131, 138-141, 146-151, 160,164, 168-174, and 178-185 are rejected under 35 U.S.C. 102(e) as being anticipated by Schneider US Patent 6,258,378.

Schneider discloses methods of delivering therapeutically active compositions comprising administering a gaseous contrast agent and a bioactive agent to a subject and then employing ultrasound energy with about 1MHz of frequency, to deliver the bioactive agent (see abstract; col 8, lines 16-45; see Example 3-4, col 13-14). Accordingly, Schneider anticipates the limitations of the instant claims.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 141, 146-151, 185 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Siegel et al US Patent 5,695,460.

Applicant argues that the instant methods are directed to delivering a bioactive agent, and Siegel's methods are directed to a different purpose and utilizes different ultrasound frequency.

In reply Examiner states that as discussed above, Siegel clearly teaches the method steps of the instant claims, accordingly absence of showing unexpected results, modifying the rate of infusion and the ultrasound frequency would have been achieved by routine experimentation.

Claims 116-131, 138-141, 146-151, 160, 164-166, 168-174, and 178-184 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Porter US Patent 5,648,098 in view of Siegel et al US Patent 5,695,460.

Applicant argues that neither of the cited references is directed to delivery of a bioactive agent. In response Examiner states that Porter specifically sets forth delivery of medicaments other than thrombolytic agents to the site of thrombosis (see col 10, lines 20-25). Porter also indicates that such medicaments may be a radiographic dye (see col 8, lin 15-16). Thus, Porter provides for the general delivery of medicaments to a site of interest. Siegel teaches delivery of thrombolytics to a thrombus. Accordingly, as suggested in previous Office Actions, the combined teachings of Porter and Siegel render the instant methods of delivery obvious, because the combined teachings of Porter and Siegel suggests the use of a ultrasonic gaseous contrast agents with a therapeutic agent to improve the therapeutic end result.

**Conclusion**

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

SS  
November 4, 2002

  
RUSSELL TRAVERS  
PRIMARY EXAMINER  
GROUP 1200